On the Reaction of 2,4-Dihydroxy-1,4-benzoxazin-3-one to 2(3)-Benzoxazolinone

ERKKI HONKANEN
and ARTTURI I. VIRTANEN

Laboratory of the Foundation for Chemical Research, Biochemical Institute, Helsinki, Finland

In earlier papers [1,2] from this laboratory it was confirmed that the aglucone, 2,4-dihydroxy-1,4-benzoxazin-3-one, isolated from crushed rye seedlings and its 7-methoxy derivative [3] from wheat and maize plants undergoes a reaction by heating in aqueous solution, upon which 2(3)-benzoxazolinone (or its 6-methoxy derivative) is formed by simultaneous liberation of formic acid. Later a similar reaction was found to occur also by heating of 4-hydroxy-1,4-benzoxazine-2,3-dione (III)[4], carbon dioxide being split off.

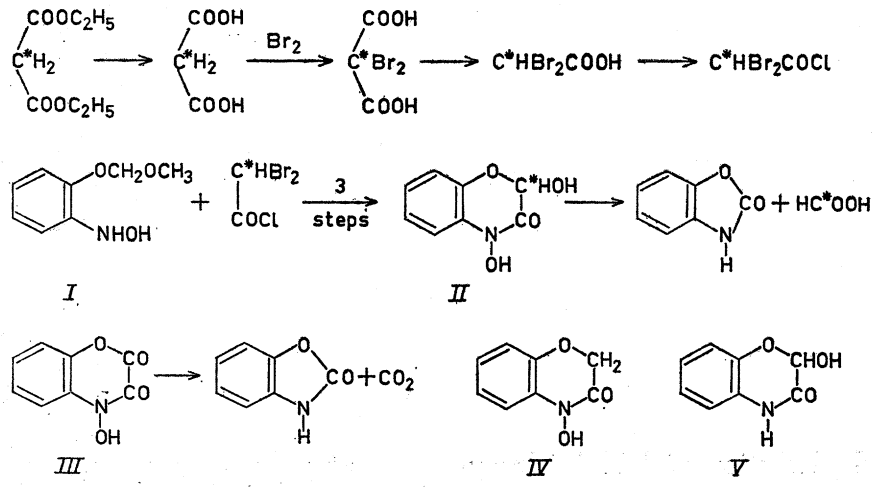
Theoretically there are two possibilities for the formation of the formic acid: from carbon atom 2 or 3. To solve this problem an aglucone (II) labelled with ^{14}C at the position 2 was synthesized by an analogous procedure as in the case of the syntheses of the normal aglucone [5] from *o*-methoxymethoxyphenylhydroxylamine (I) and dibromoacetyl-2-^{14}C chloride. The needed dibromoacetyl-2-^{14}C chloride was prepared by the following reactions from diethyl-(malonate-2-^{14}C).

After heating the aqueous solution of II, the radioactivity was found in the formic acid, and we conclude that the formic acid originates from carbon atom 2 in II. Nothing certain can be said about the reaction mechanism. A prerequisite for this reaction seems to be the easy rupture of the bond between the oxygen and carbon atom 2 and the presence of the N-hydroxyl group. The compound IV [4] which has a simple ether linkage and the compound V [5] which has no N-hydroxyl group are quite stable in boiling aqueous solution.

Dibromoacetyl-2-^{14}C chloride. A mixture of 1.85 mg (0.025 mC) of diethyl-(malonate-2-^{14}C)* and 500 mg of diethylmalonate in 10 ml of 2 N hydrochloric acid was heated for 24 h at 50°C. The solution was then evaporated to dryness under reduced pressure. The residue was dissolved in 1 ml of 2 N hydrochloric acid, the solution cooled below +5°C, and 350 μl of bromine were added. After standing for 2 h the solvent was evaporated in vacuum. The residue (dibromomalonic acid) was then decarboxylated to dibromoacetic acid by heating for 1 h at 130°C. Two ml of thionyl chloride were added after cooling, and the mixture was boiled for 1 h on a water bath. The excess of thionyl chloride was then removed under reduced pressure, and the residue was used without further purification for the following reaction.

2,4-*Dihydroxy*-1,4-*benzoxazin*-3-*one*-2-^{14}C. A solution of the above dibromoacetyl-2-^{14}C chloride in 10 ml of dry ether was added under cooling to a solution of *o*-methoxymethoxyphenylhydroxylamine prepared from 0.5 g of *o*-

* A product of The Radiochemical Centre.



methoxymethoxynitrobenzene [5] in 10 ml of dry ether. The preparation was then carried out by a similar procedure as in the case of the synthesis of 2,4-dihydroxy-1,4-benzoxazin-3-one [5], with the difference that the reaction time with methanol-hydrochloric acid was reduced from 30 min to 10 min and that with the sodium hydroxide solution from 2 h to 20 min. The yield was by this means increased about three times. The product was crystallized from a mixture of ethyl acetate-petroleum ether. Total yield (from diethylmalonate) 21 mg (3.7 %).

Conversion of 2,4-dihydroxy-1,4-benzoxazin-3-one-2-^{14}C to benzoxazolinone. 21 mg of the 2-^{14}C-labelled aglucone was dissolved in 1 000 ml of water and heated for 30 min at 100°C. 10 mg of sodium hydrogen carbonate was added and the cooled solution extracted 4—5 times with ether. The water solution as well as the ether extract were evaporated to dryness under reduced pressure. The radioactivity was then measured in both residues. The activity of the sodium formate fraction was about 20 times higher than that of the benzoxazolinone fraction. The low activity which was obtained in benzoxazolinone may be due to the coloured impurities formed as by-products in the reaction.

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1. Virtanen, A. I. and Hietala, P. K. *Acta Chem. Scand.* **14** (1960) 499.
2. Hietala, P. K. and Virtanen, A. I. *Ibid.* **14** (1960) 502.
3. Wahlroos, Ö. and Virtanen, A. I. *Ibid.* **13** (1959) 1906.
4. Honkanen, E. and Virtanen, A. I. *Ibid.* **14** (1960) 1214.
5. Honkanen, E. and Virtanen, A. I. *Ibid.* **14** (1960) 504.

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